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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,944	04/13/2004	Ivan Michael Richards	PC27679A	5448

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER

SPIVACK, PHYLLIS G

ART UNIT PAPER NUMBER

1614

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/823,944	RICHARDS ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 3-22 is/are rejected.
- 7) ☒ Claim(s) 1 and 2 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5-24-04</u> . | 6) <input type="checkbox"/> Other: ____. |

Art Unit: 1614

An Information Disclosure Statement filed May 24, 2004 is acknowledged and has been reviewed.

Claims 1-22 are presented and represent all of the claims under consideration.

The disclosure is objected to for the following informality: In claim 19, in addition to various salts of the recited compounds, such as bromide, iodide and chloride, the next to the last compound is capitalized.

Appropriate correction is required.

Claims 6-8, 12, 14-16, 18 and 19 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims only in the alternative. See MPEP § 608.01(n).

Claims 3 and 5-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to the treatment of IBS comprising administering a compound or a stereoisomer of Formula III or V. The specification provides support for treating IBS comprising administering a compound of instant formula I or II.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 where the court set forth factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided

Art Unit: 1614

- 3) the presence or absence of working examples
- 4) the nature of the invention
- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to treatment of IBS comprising administering quaternary ammonium compounds of various formulae as antimuscarinic agents.

The relative skill of those in the art is generally that of a Ph.D. or M.D. with expertise in the area of gastroenterology.

A successful treatment modality employing one particular quaternary ammonium compound for use in the treatment of IBS does not presage success with others.

The breadth of the claims

The claims are not unduly broad.

The amount of direction or guidance provided and the presence or absence of working examples

Art Unit: 1614

There are no working examples drawn to the administration of compounds of instant formulae III and V.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to operability of various quaternary ammonium compound of diverse structure. The skilled artisan would expect the interaction of a particular compound in the treatment of IBS to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for each agent. While it is known in the prior art that quaternary compounds exhibit an increased residence time in the gut relative to non-quaternized forms, the instant specification sets forth no suggestion that any such compound would prove efficacious in the treatment of IBS. Absent reasonable *a priori* expectations of success for using a particular quaternary ammonium compounds to treat IBS, one skilled in the gastroenterology arts would have to test extensively many compounds to discover which demonstrate efficacy. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4 and 6-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Takeuchi et al., U.S. Patent 6,017,927.

Takeuchi teaches the administration of a compound of instant claim 4 having a quaternary nitrogen for use in the treatment of irritable bowel syndrome. See Example 18, column 2. See column 3, lines 48 and 62, and column 9, lines 8-12 and 60. Dosages, optimal dosage regimens and modes of administration are disclosed in columns 11-12.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 5-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuchiya et al., U.S. Patent 5,948,792, in view of Remington's Pharmaceutical Sciences.

Tsuchiya teaches the administration of a compound of instant claim 5, absent a quaternary ammonium group, for use in the treatment of irritable bowel syndrome. See the Abstract. Remington teaches the advantageous formulation of agents having a quaternary ammonium to prevent penetration of a drug through the blood brain barrier and, therefore, avoid central nervous system side effects. Therefore, in view of the combined teachings of Tsuchiya and Remington, one skilled in the art of formulation chemistry would have been motivated to prepare a quaternized form of a medicament that had previously demonstrated efficacy in the treatment of IBS in a non-quaternized

Art Unit: 1614

form, with a reasonable expectation of providing the same desired therapeutic effect without unwanted adverse effects.

Yoshiyama, M., Current Opinion in Central & Peripheral Nervous System Investigational Drugs, Kobayashi et al., Japanese Journal of Pharmacology, Richards et al., U.S. Patent 6,890,920, and Cross et al., U.S. Patent 5,096,890, are cited to show further the state of the art. Yoshiyama teaches the administration of a compound designated UK-88525, which lacks a quaternary ammonium and an additional group attached to the pyrrolidinyll nitrogen, for use in the treatment of IBS. Kobayashi teaches the administration of a compound of instant claim 4 as a muscarinic M3-receptor antagonist, absent a quaternary ammonium and an additional group attached to the quinuclidinyll nitrogen, for use in the treatment of irritable bowel syndrome. Cross teaches the administration of a compound close in structure to that of instant claim 2, a muscarinic receptor antagonist, absent a quaternary ammonium, for use in the treatment of diseases characterized by altered motility and/or tone of smooth muscle, such as for irritable bowel syndrome. Richards teaches the administration of the compound of instant claim 1, as an antimuscarinic agent, but not as an agent in the treatment of IBS.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

Art Unit: 1614

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low, can be reached 571-272-951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 5, 2006



Phyllis G. Spivack

1614 **PHYLLIS SPIVACK**
PRIMARY EXAMINER